Challenges in Non-Clinical Testing of Hemostatic Medical Devices for Trauma Use

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Various Compositions of Hemostatic Devices

- Animal Tissue (e.g., Collagen, Gelatin, Chitosan, Thrombin)
- Derived from Plants (e.g,. Alginate)
- Mineral-Based (e.g., Kaolin, Zeolite)
- Synthetics (e.g., Polyester, Carboxymethylcellulose)





Issues with Animal Source Material

Sourcing Issues

- Animal Husbandry
- Control of Tissue Collection
- Manufacturing Controls for Animal Tissue Components
- Sterilization (and Virus Validation Studies)

Medical Devices Containing Materials
Derived from Animal Sources
(Except for In Vitro Diagnostic Devices) (Draft)

http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm381379.ht



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Considerations for Non-Clinical Testing

For Potential Battlefield Products

- Consider Environmental Conditions
 - Temperature
 - Altitude
 - . Humidity
 - Robustness of Packaging
- Consider the User
 - Labeling revisions based on bench/animal experience

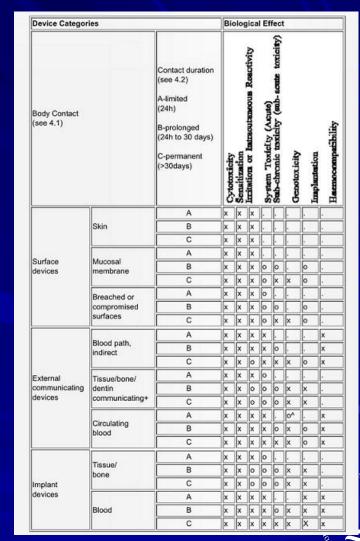




Biocompatibility - Use of ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing" - Draft Guidance 2013

Series of standardized tests

- Dependent on:
 - Time of contact
 - Type of contact
- Works for many, but not all biomaterials





Biocompatibility - Use of ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing" - Draft Guidance 2013

Points of Interest (pp. 9 – 13)

- Final Product or Representative Sample?
- In Situ Polymerizing Material
- Bioabsorbable Material
- Biological Response Resulting from Device Mechanical Failure
- Submicron or Nanotechnology Components
- Multiple components or materials in a single sample



Biocompatibility- Use of ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing" - Draft Guidance 2013

Sources of Information

- In-house studies
- Master Files from Raw Material Suppliers
- Published Literature
- Others? (e.g., MSDS)





- Final Product or Representative Sample?
 - Animal Tissue / Scaffold construct
 - Sealant / Patch Crosslinked in situ
 - Surgical Instrument Models for TSE

"Certain instrument features are particularly difficult to clean – hinges, mated surfaces and lumens. Many TSE investigators are now using small (5 mm) stainless steel wires coated with inoculum in their studies of TSE transmissibility. The material is a suitable stand-in for many instruments."

(page 7 – FDA Briefing Material 9/27/05 – Panel Mtg.





- In Situ Polymerizing and Bioabsorbable Materials
 - Consider the Reagents
 - Consider the Reaction
 - Consider the Final Product
 - Consider the Decomposition Products
 - Kinetics of Resorption





Submicron or Nanotechnology Components

- Unique properties of submicron / nanotechnology components, (e.g., large surface area / particle, aggregation, agglomeration, immunogenicity, toxicity (altered release kinetics?)
- Rationally designed features that modify host cell response.





Submicron or Nanotechnology Components

Consider:

- Careful characterization of the test sample and extract conditions (e.g., solvent type) to avoid non-clinically relevant testing artifacts
- Assure that the test article is representative of the clinical product





Resources

Device Search Engines

PMA/510k/MAUDE http://www.fda.gov/cdrh/databases.html

CDRH - Guidance Database Search Engine

http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm

Use of International Standard ISO-10993, "Biological Evaluation of Medical Devices Part 1: Evaluation and Testing" (Draft)

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM348890.pdf

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